Postprandial duodenal function in man[1]

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SUMMARY   Duodenal function was studied in 11 healthy volunteers after intragastric instillation of a mixed semi-elemental meal. The duodenum accepted chyme of varying pH, osmolality, and nutrient concentration; and, as a result of biliary, pancreatic, and enteric secretion as well as absorption, it delivered chyme with nearly constant pH, osmolality, and nutrient concentration to the jejunum. The flow rate and nutrient load of jejunal chyme varied. The duodenum absorbed more carbohydrate than lipid and less protein, taking up each nutrient at a constant rate during most of the postprandial period. The percentage of nutrient load absorbed was greatest in the late postprandial period, when flow rate, nutrient load, and concentrations were low.

Duodenal chyme influences all major functions of the duodenum; yet postprandial chyme in normal man has not been fully characterised. Duodenal hormonal and neural regulation of gastric, pancreatic, and biliary secretion and of upper gastrointestinal motor activity is sensitive to chyme nutrient content (Windsor *et al.*, 1969), osmolality (Meeroff *et al.*, 1975), and pH (Johnston and Duthie, 1966). Pancreatic and biliary secretions that are important to digestion mix with chyme in this segment of bowel and are similarly sensitive to the characteristics of chyme. An example of this is seen in the Zollinger-Ellison syndrome, where duodenal delivery of an acidic chyme inactivates lipase and precipitates bile acids, thus producing steatorrhoea (Go *et al.*, 1970). Also, duodenal absorption and secretion of fluid and electrolytes and absorption of nutrients are certainly dependent on the composition of duodenal chyme. This is apparent in considering the dumping syndrome (Abbott *et al.*, 1960).

Little information has been obtained from normal man to characterise the postprandial gastric contents delivered into the duodenum, the modifications of this chyme that occur along the duodenum, and the chyme that is delivered into the jejunum. We have tried to develop more thorough knowledge of these substances and changes and of the nutrient absorption taking place at this level of the bowel after ingestion of a liquid, mixed, semi-elemental meal. Although this meal might not induce the same duodenal events as a more complex one, it was used to simplify analytical procedures.

Methods

SUBJECTS

Eleven healthy volunteers (two female and nine male, aged 21 to 62 years) participated in 16 studies after giving informed consent. All data reported as results are from the initial study performed in each of the 11 subjects. The five duplicate studies are used only to provide further independent assessment of the correlation between emptying of nutrient and of meal marker in a particular study.

MEAL

A 400-ml standard liquid meal containing about 300 calories distributed as 40% carbohydrate, 40% lipid, and 20% protein (similar to their distribution in the normal American diet) was used. The nutrients were semi-elemental, in forms normally appearing in the bowel lumen, which could be assimilated easily and which permitted simple analysis of intestinal chyme for nutrient composition. The meal was prepared by dissolving in water 30·7 g maltose (0·224 molar), 14 g oleic acid (0·124 molar), 16·4 g of a complete tryptic hydrolysate of casein, and 15 g of a nonabsorbable marker (polyethylene glycol 4000) and adjusting the pH to 7·0 with a small amount of NaOH. Sonication for 10 minutes produced an emulsion with osmolality 544 ± 5 mOsm/l which was stable for several hours, thus longer than the study period.

TUBES

Two peroral tubes were used (Fig. 1). For the duodenum, there was a sump tube that ran to a mercury-weighted tip beyond an occlusive balloon and had three small polyvinyl tubes cemented to it. This assembly (of total external diameter, except for the balloon, of approximately 6 mm) provided (1) the duodenal perfusion site; (2) an aspiration site with an air channel, to facilitate suction, located 20 cm distal to the perfusion site; (3) an inflatable balloon immediately distal to the aspiration site; and (4) an aspiration site immediately beyond the balloon. Gastric sampling was done *via* a separate 14-F sump tube.

PROCEDURE

Each study was begun after an overnight fast. The volunteers were seated in an upright position throughout the study. Under fluoroscopic control, the duodenal tube was positioned with the balloon at the ligament of Treitz and the gastric tube was positioned with its tip in the most dependent area of the antrum. Duodenal perfusion with ^{14}C-PEG (polyethylene glycol, specific activity 0·5 μCi/mg) dissolved in 0·15 M NaCl was maintained at 2 ml/min throughout the study period. The occlusive balloon was inflated with 30 to 45 ml of air until the subject sensed its presence, without having any discomfort. Total occlusion was confirmed by demonstrating that neither bile nor ^{14}C-PEG was present distal to the balloon. More than 92% of marker was recovered proximal to the balloon in all studies. No study was included in which duodenal-gastric reflux of duodenal marker exceeded 15%.

Fasting gastric and duodenal collections were made by continuous suction (-25 mm Hg) during two 10-minute intervals.

Then the meal was injected *via* the gastric tube over eight minutes, and gastric and duodenal samples were collected for two hours after the meal. Every 10 minutes, 200 ml of gastric contents was aspirated, a 10-ml aliquot was taken from it, and the remainder was returned immediately to the stomach. The aliquots from each 30-minute interval were pooled.

Duodenal samples were aspirated by continuous suction (-25 mm Hg), collected over ice, and pooled at 30-minute intervals. No duodenal chyme was reinfused. To correct for transit time, duodenal collections were begun five minutes after corresponding gastric collections.

At the end of the study period, gastric contents were aspirated completely; then 200 ml of a normal saline gastric wash was injected over five minutes; and this was aspirated, to recover as much of the marker as possible.

Determinations of osmolality (Wescor 5100 Vapor Pressure Osmometer) and pH (Fisher 520 Digital pH/Ion Meter) were performed immediately on all gastric and duodenal samples. Marker concentrations also were measured in all samples (Brunner *et al.*,
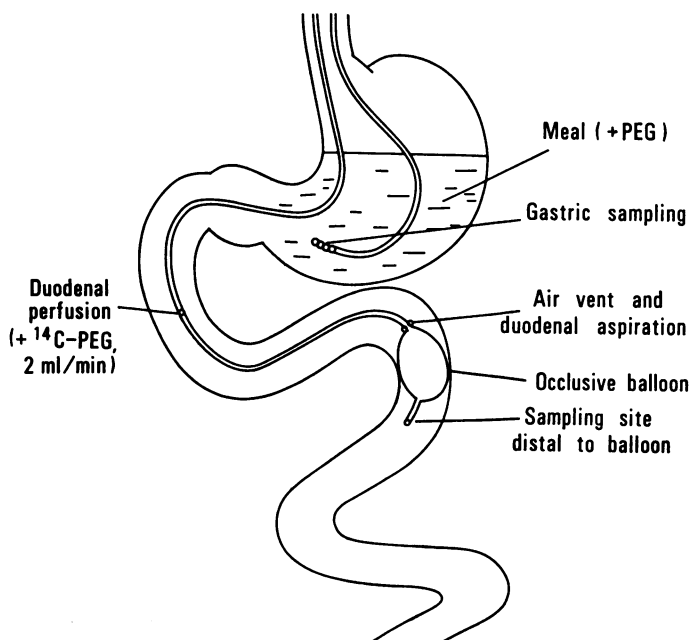

Meal (+PEG)

Gastric sampling

Duodenal perfusion (+ ^{14}C-PEG, 2 ml/min)

Air vent and duodenal aspiration

Occlusive balloon

Sampling site distal to balloon

Fig. 1   *Peroral gastric sump tube and multiluminal duodenal assembly, as placed for use.*

1974), and bilirubin and trypsin concentrations were measured in all duodenal samples (Brunner *et al.*, 1974). Bilirubin and trypsin outputs as well as the gastric volume emptied and meal emptied were calculated as previously reported (Brunner *et al.*, 1974; Malagelada *et al.*, 1976). The formulas were modified to include the actual volume collected at the ligament of Treitz rather than a flow rate previously calculated from the duodenal perfusate (Malagelada *et al.*, 1976; Clain *et al.*, 1977). Therefore, characterisation of gastric contents emptied into the duodenum was indirect (based on marker determinations), and that of chyme leaving the duodenum was measured directly.

Total protein was determined by the method of Lowry *et al.* (1951), fatty acid by the method of Cohen *et al.* (1969), carbohydrate by analysis of maltose (Bernfeld, 1955), and glucose by the hexokinase method (Bergmeyer *et al.*, 1974). In the maltose assay, correction was made for free glucose present. Nutrient assays were performed on the meal, all duodenal samples, and the gastric contents aspirated at the end of the two-hour study period. Although we cannot be sure that we were measuring only exogenous nutrient, the contribution by endogenous secretions probably was very small.

VALIDATION STUDY
In an attempt to determine the maximal potential interference, a validation study was performed in which pancreatic and biliary secretions aspirated from five normal subjects at the time of maximal cholecystokinin stimulation were analysed for carbohydrate, lipid, and protein by the same techniques mentioned above. As proportions of the mean postprandial concentrations at the ligament of Treitz in the main study, the highest concentrations in the validation study were carbohydrate 3·5%, lipid 9·5%, and protein 15·1%. Adibi and Mercer (1973) also have shown that dietary protein makes up the major portion of intraluminal amino acids and peptides after a meal.

STATISTICAL METHODS
Paired sets of data from individuals were analysed by the paired *t* test (Dixon and Massey, 1969).

Results

PH AND OSMOLALITY
After ingestion of the meal (pH 7·0), the pH of gastric contents—and therefore of chyme delivered into the proximal duodenum—decreased progressively (each point different from preceding point, $p < 0.01$). The pH at the distal end of the duodenum (aspirated at the ligament of Treitz) was quite

stable, however, close to neutrality (Fig. 2). Osmolality of the chyme behaved similarly: after the meal (osmolality 544), gastric osmolality progressively decreased toward the osmolality of blood (each point different from preceding point, $p < 0.01$). This steady decline of the osmolality of gastric contents entering the duodenum was not reflected by chyme at the ligament of Treitz, where osmolality remained stable near isotonicity (Fig. 2).
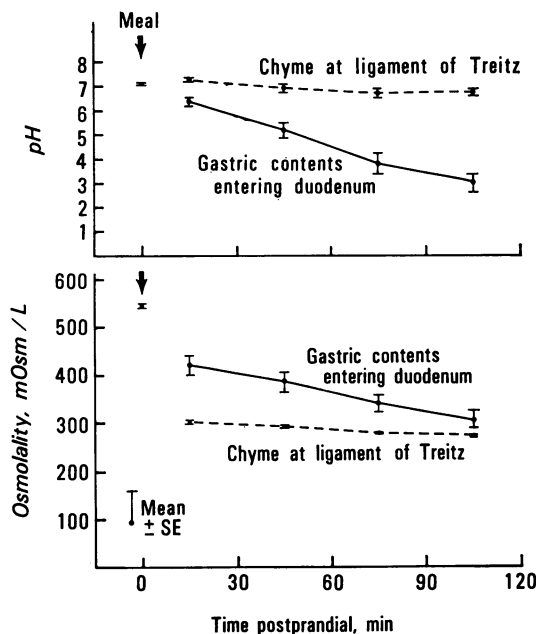

Fig. 2 *Simultaneously measured postprandial pH and osmolality of gastric contents entering duodenum* (——) *and chyme leaving duodenum at ligament of Treitz* (– – –). *Points plotted at zero time represent pH and osmolality of meal.*

VOLUME FLOW
Figure 3 demonstrates volume flows. The total volume of gastric contents emptied into the duodenum during each 30-minute interval was constant throughout the two-hour postprandial period (no point different from any other at $p < 0.05$ level). The actual meal volume emptied into the duodenum was greatest in the first 30 minutes, then progressively less in each interval thereafter as diluting gastric secretion became a greater proportion of the gastric volume emptied (each point different from preceding point, $p < 0.01$). Throughout the study period, the volume flow at the ligament of Treitz was greater than that entering the duodenum ($p < 0.01$). The net change of chyme volume along the duodenum is represented by
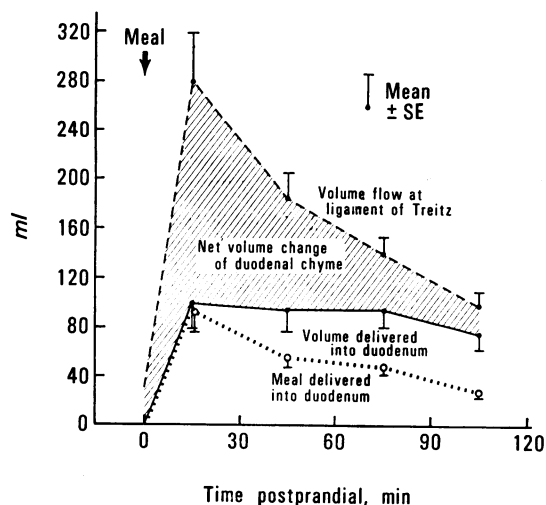
Fig. 3 *Simultaneously measured postprandial volume being delivered into duodenum* (———) *and volume leaving duodenum at ligament of Treitz* (– – –), *with shaded area between these curves representing net volume change of duodenal chyme. Also plotted* (· · · ·) *is portion of volume delivered into duodenum which represents meal volume rather than gastric secretions.*

the area between the curves representing volume delivered into the duodenum and volume at the ligament of Treitz. This net difference was greatest early in the postprandial period and decreased progressively (each point different from preceding point, P < 0·01).

NUTRIENT LOADS AND CONCENTRATIONS
The meal administered is a stable emulsion; and the

protein, lipid, and carbohydrate were emptied from the stomach in the same proportions as administered —and in stable proportion to the meal marker. Figure 4 demonstrates the correlations among the meal marker, protein, lipid, and carbohydrate emptied over two hours, expressed as percentages of the marker or nutrient administered. (All values were calculated from actual measurements of residual gastric volume and of meal marker or nutrient concentrations.) These correlations validate our use of meal marker to calculate nutrient loads and concentrations entering the duodenum.

All nutrient loads and concentrations delivered into the duodenum were maximal in the early postprandial period and decreased progressively (Fig. 5; each point different from preceding point, P < 0·05). The duodenum handled the three nutrients differently, however, absorbing more carbohydrate than lipid and less protein, and therefore delivering less carbohydrate than lipid and more protein to the jejunum. Consequently, separate lines are drawn to represent the different nutrient loads and concentrations at the level of the ligament of Treitz. The nutrient *loads* arriving at the ligament of Treitz were largest in the early postprandial period and diminished progressively (each point different from preceding point, except lipid and carbohydrate at 75 and 105 min, P < 0·05). The nutrient *concentrations*, however, had stabilised; and there was no change of protein or lipid concentration in chyme between any 30-minute intervals in the study period (no point different from any other, at P < 0·05 level). The carbohydrate concentration in chyme at the ligament of Treitz, although much more stable than at the pylorus, gradually decreased (each point different
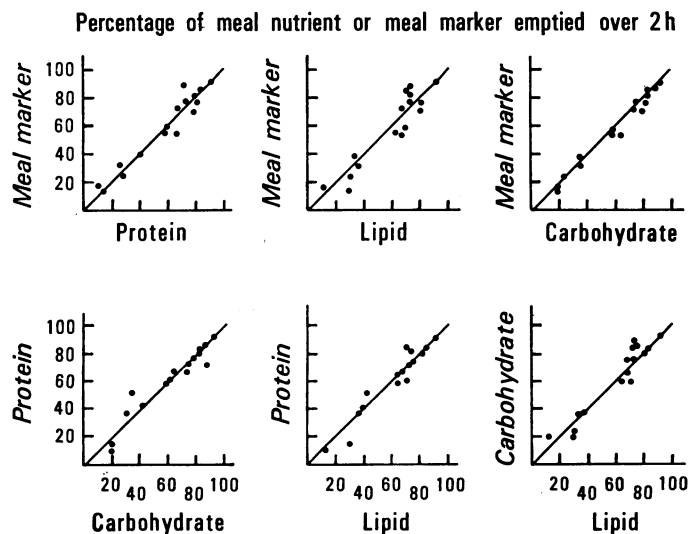
Percentage of meal nutrient or meal marker emptied over 2 h

Fig. 4 *Correlations between meal marker, protein, lipid, and carbohydrate emptied from stomach over two-hour postprandial study period, expressed as percentage of meal marker or corresponding meal nutrient. Each point represents a single study. Lines drawn are the lines of identity. Correlation coefficients range from 0·92 to 0·99, all being significant* (P < 0·001).
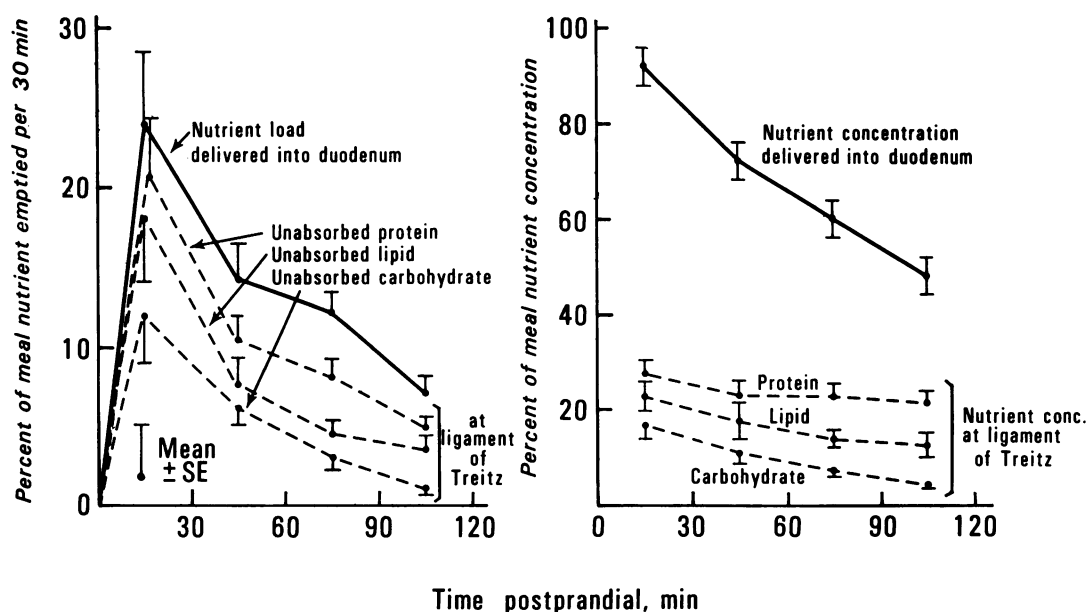
Fig. 5 *Postprandial nutrient loads (left) and concentrations (right) in chyme entering and leaving duodenum. Solid lines represent percentage of each meal nutrient volume or concentration being delivered into the duodenum. Only one line is drawn, since protein, lipid, and carbohydrate are emptied from stomach in stable proportion to one another after this meal. Dashed lines represent percentage of each meal nutrient or concentration in meal reaching ligament of Treitz. Differences in duodenal handling of nutrients necessitates drawing of three lines.*

from preceding point, P < 0·05) because the duodenum absorbed a much greater proportion of this nutrient than of protein or lipid. Actual concentrations of each nutrient in chyme at the ligament of Treitz after this meal were: protein 9·71 ± 0·53 mg/ml, lipid 5·79 ± 0·56 mg/ml (20 mM), carbohydrate 7·22 ± 0·82 mg/ml (21 mM). During the two-hour study period, mean absorptions were 23 ± 6% of the protein load, 41 ± 9% of the lipid, and 62 ± 9% of the carbohydrate (differences significant, P < 0·01).

NUTRIENT ABSORPTION
Duodenal nutrient handling is further demonstrated in Fig. 6. During the first 90 minutes postprandially, the amounts of each nutrient absorbed and, therefore, the rates of absorption (protein 0·68 ± 0·10, lipid 0·95 ± 0·09, carbohydrate 2·81 ± 0·24 g/30 min) were constant despite changes in nutrient loads, nutrient concentrations, and flow rates (no point different from any other at P < 0·05 level). The quantities of each nutrient absorbed decreased in the final 30 minutes as the nutrient load decreased (P < 0·05). The percentage of the nutrient load absorbed each 30 minutes, a measure of absorptive efficiency, increased through the first three 30-

minute postprandial intervals (each point different from preceding point, P < 0·05).

PANCREATIC AND BILIARY OUTPUTS
Trypsin and bilirubin outputs are demonstrated in Fig. 7. Pancreatic enzyme output was maximal in the first 30 minutes postprandially and declined steadily thereafter. Bilirubin output, reflecting gallbladder contraction, also was maximal in the first 30 minutes; but thereafter it fell off faster than trypsin output.

Discussion

Isolation of the gastroduodenal field permitted study of the coordinated upper gastrointestinal events that occur in the postprandial period in normal man, making possible the determination of proximal and distal duodenal nutrient loads, amount of nutrient absorbed, and percentage of nutrient load absorbed from duodenal chyme in its normal postprandial form. Previous studies of duodenal absorption have utilised either isolated nutrient infusions (Abbott *et al.*, 1940; DiMagno *et al.*, 1971) or comparison of nutrient concentration with nonabsorbable marker concentration, a technique permitting calculation of
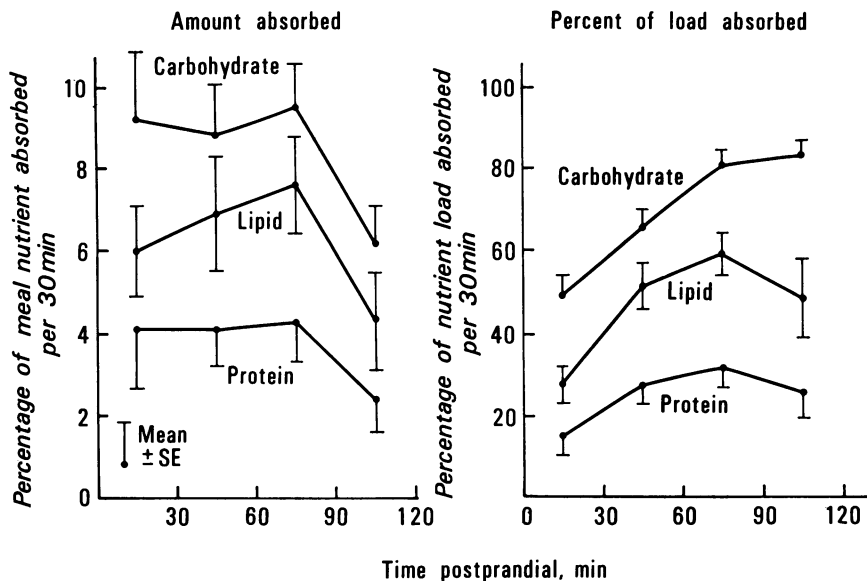
Amount absorbed   Percent of load absorbed

Fig. 6   *Postprandial duodenal absorption of each nutrient expressed as percentage of that nutrient in meal administered (left). Efficiency of absorption of each nutrient is expressed as percentage of that nutrient load absorbed (right).*
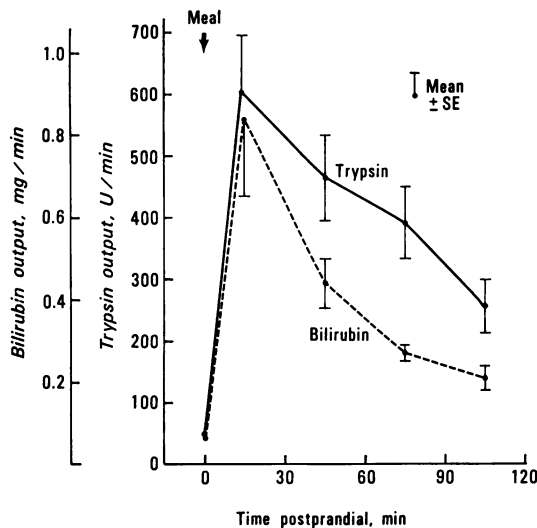

Fig. 7   *Postprandial trypsin and bilirubin outputs.*

percentage absorption but not nutrient load (Borgström *et al.*, 1957). Although permitting these further observations, this study may not be directly comparable with studies in which chyme either was not diverted or was reintroduced, because of the recognised jejunal phase of gastric function (Clain *et al.*, 1977).

Gastric contents entering the duodenum after a

meal have progressively decreasing pH, osmolality, and nutrient concentration as the stomach dilutes the meal with acidic, near-isotonic gastric secretion and, at the same time, meal buffer is being emptied. Mechanisms to modify the chyme between its emptying from the stomach and its delivery to the jejunum include enteric, biliary, and pancreatic secretion as well as duodenal absorption. Consequently, the chyme delivered to the ligament of Treitz after this meal has constant pH near neutrality and constant osmolality near isotonicity. Fordtran and Locklear (1966) reported similar findings with a solid, complex, meal. Individual nutrient concentrations also become fairly constant before reaching the ligament of Treitz.

In contrast, nutrient and volume loads at the ligament of Treitz change during the postprandial period. This reflects nutrient rather than volume delivery into the duodenum, since the rate of gastric volume emptying is constant throughout the study period.

Throughout the study period, the volume flow at the ligament of Treitz is greater than that entering the duodenum, with its greatest net increase occurring early postprandially. Pancreatic and biliary secretions contribute significantly to this increase of chyme volume. Pancreatic and biliary secretion is maximal early, when maximal nutrient loads and concentrations are being delivered into the duodenum, and decrease as the nutrient loads and concentrations

decrease. It is of interest that both trypsin and bilirubin outputs progressively decrease, while the amount of each nutrient absorbed remains constant. Although the early peaks of apparent output may represent a washout phenomenon, the output curves do not stabilise as would be expected if they were controlled only by absorbed nutrient.

Another reason for the large early net increase in duodenal volume is the limited amount of nutrient absorption. The greatest percentage of the nutrient load is absorbed in the third 30-minute postprandial interval, when flow rates, loads, and concentrations are less. Also, little duodenal fluid absorption can be expected early in the postprandial period, when chyme from the stomach is hypertonic and flows through the duodenum rapidly.

Despite the changes of nutrient loads, nutrient concentrations, and flow rates, the amount of each nutrient absorbed by the duodenum per 30 minutes is constant through two hours postprandially. More carbohydrate than lipid is absorbed, and less protein.

Borgström *et al.* (1957) also have investigated nutrient absorption from a mixed meal containing skim milk, dextrose, corn oil, and albumin. Nutrient absorption was found to be complete in the proximal 50 to 100 cm of jejunum, with lipid absorbed more proximally than protein or carbohydrate. Amounts of protein and lipid absorbed proximal to the ligament of Treitz in that study were similar to the amounts absorbed in ours, but carbohydrate absorption was quite different.

The reason for this difference is uncertain. The two studies used different forms of carbohydrate. Maltose, used in our study, is well absorbed—at least in the jejunum: 60% of a 72-mM/h infusate is absorbed by a 30-cm segment of jejunum (Gray and Santiago, 1966). Cook (1973) found greater absorption of carbohydrate from maltose than from glucose perfused in the human jejunum. Dahlqvist and Borgström (1961), however, found little absorption or hydrolysis of maltose in the duodenum. In the study of Borgström *et al.* (1957), 27% of the carbohydrate was in the form of lactose, a disaccharide requiring hydrolysis before absorption (Gray and Santiago, 1966). But maltose can be absorbed intact, even though its rate of hydrolysis is about twice that of lactose (Gray and Santiago, 1966).

In our study, the rate of lipid absorption was between the rates of carbohydrate and protein absorption. Conditions should have been ideal for absorption, since bile was permitted to mix with duodenal chyme in a physiological manner to form micelles. Pancreatic lipase was not necessary for digestion, because the source of lipid used was a fatty acid.

The nutrient absorbed most slowly was the pro-

tein, despite its presentation as small peptides, a form that should maximise its absorption rate (Adibi, 1971; Crampton *et al.*, 1971; Adibi *et al.*, 1975). Although actual analysis of amino acids and peptides was not performed, characterisation of these in similar tryptic hydrolysates demonstrates an average peptide length of 2·2 amino acid units (Crampton *et al.*, 1971). This is similar to the form of protein normally found in the intestinal lumen (Adibi and Mercer, 1973). Normally, in fact, meal protein is found as far distally as the mid-ileum (Adibi and Mercer, 1973).

In summary, in the postprandial period after a liquid semi-elemental meal, the normal human duodenum receives chyme of varying pH, osmolality, and nutrient concentration; and as a result of biliary, pancreatic, and enteric secretion as well as absorption, it delivers chyme with near constant pH, osmolality, and nutrient concentration to the jejunum. Jejunal chyme varies in flow rate and nutrient load. Duodenal conditions permit maximal absorption of each nutrient over the first 90 minutes postprandially, and more carbohydrate than lipid and less protein is absorbed. The percentage of nutrient load absorbed is greatest in the late postprandial period when flow rates, nutrient load, and concentrations are low. How these results are modified by meals of different size, composition, and physical state will need to be evaluated in the future.

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